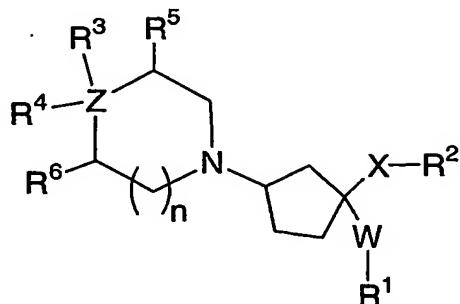


WHAT IS CLAIMED IS:

1. A compound of the formula I:



5

I

wherein:

X is selected from the group consisting of:

-NR¹⁰-, -O-, -CH₂O-, -CONR¹⁰-, -NR¹⁰CO-, -CO₂-, -OCO-,
 -CH₂(NR¹⁰)CO-, -N(COR¹⁰)-, -CH₂N(COR¹⁰)-, phenyl, and

10 C₃-6 cycloalkyl,

where R¹⁰ is independently selected from: hydrogen, C₁-6 alkyl, benzyl,
 phenyl, and C₁-6 alkyl-C₃-6 cycloalkyl,

which is unsubstituted or substituted with 1-3 substituents where the
 substituents are independently selected from: halo, C₁-3alkyl,

15 C₁-3alkoxy and trifluoromethyl;

W is selected from:

phenyl and heterocycle, which is unsubstituted or substituted with 1-3
 substituents where the substituents are independently selected from:

20 halo, C₁-3alkoxy and trifluoromethyl;

Z is selected from:

C, N, and -O-, wherein when Z is N, then R⁴ is absent, and when W is -O-,
 then both R³ and R⁴ are absent;

25

n is an integer selected from 0, 1, 2, 3 and 4;

R^1 is selected from:

- (a) halo,
- (b) trifluoromethyl,
- (c) trifluoromethoxy,
- 5 (d) hydroxy,
- (e) C_1 -6alkyl,
- (f) C_3 -7cycloalkyl,
- (g) $-O-C_1$ -6alkyl,
- (h) $-O-C_3$ -7cycloalkyl,
- 10 (i) $-SCF_3$,
- (j) $-S-C_1$ -6alkyl,
- (k) $-SO_2-C_1$ -6alkyl,
- (l) phenyl,
- (m) heterocycle,
- 15 (n) $-CO_2R^9$,
- (o) $-CN$,
- (p) $-NR^9R^{10}$,
- (q) $-NR^9-SO_2-R^{10}$,
- (r) $-SO_2-NR^9R^{10}$, and
- 20 (s) $-CONR^9R^{10}$
- (t) $-NHC(=NH)NH_2$, and
- (u) hydrogen,

R^2 is selected from:

- 25 (C₀-6alkyl)-phenyl and (C₀-6alkyl)-heterocycle,

where the alkyl is unsubstituted or substituted with 1-7 substituents

where the substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- 30 (c) $-O-C_1$ -3alkyl,
- (d) trifluoromethyl, and
- (e) $-C_1$ -3alkyl,

and where the phenyl and the heterocycle is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- (a) halo,
- 5 (b) trifluoromethyl,
- (c) trifluoromethoxy,
- (d) hydroxy,
- (e) C₁-6alkyl,
- (f) C₃-7cycloalkyl,
- 10 (g) -O-C₁-6alkyl,
- (h) -O-C₃-7cycloalkyl,
- (i) -SCF₃,
- (j) -S-C₁-6alkyl,
- (k) -SO₂-C₁-6alkyl,
- 15 (l) phenyl,
- (m) heterocycle,
- (n) -CO₂R⁹,
- (o) -CN,
- (p) -NR⁹R¹⁰,
- 20 (q) -NR⁹-SO₂-R¹⁰,
- (r) -SO₂-NR⁹R¹⁰, and
- (s) -CONR⁹R¹⁰;

R³ is -(C₀-6alkyl)-phenyl,

25 where the alkyl is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- (c) -O-C₁-3alkyl, and
- 30 (d) trifluoromethyl,

and where the phenyl is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- (a) halo,
- (b) trifluoromethyl,

- (c) hydroxy,
- (d) C₁₋₃alkyl,
- (e) -O-C₁₋₃alkyl,
- (f) -CO₂R⁹,
- 5 (g) -CN,
- (h) -NR⁹R¹⁰, and
- (i) -CONR⁹R¹⁰;

R⁴ is selected from:

- 10 (a) hydrogen,
- (b) hydroxy,
- (c) C₁₋₆alkyl,
- (d) C₁₋₆alkyl-hydroxy,
- (e) -O-C₁₋₃alkyl,
- 15 (f) -CO₂R⁹,
- (g) -CONR⁹R¹⁰, and
- (h) -CN;

or where R³ and R⁴ may be joined together to form a ring which is selected from:

- 20 (a) 1H-indene,
- (b) 2,3-dihydro-1H-indene,
- (c) 2,3-dihydro-benzofuran,
- (d) 1,3-dihydro-isobenzofuran,
- (e) 2,3-dihydro-benzothiofuran, and
- 25 (f) 1,3-dihydro-isobenzothiofuran,

or where R³ and R⁵ or R⁴ and R⁶ may be joined together to form a ring which is phenyl,

wherein the ring is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

- 30 (a) halo,
- (b) trifluoromethyl,
- (c) hydroxy,
- (d) C₁₋₃alkyl,
- (e) -O-C₁₋₃alkyl,
- 35 (f) -CO₂R⁹,

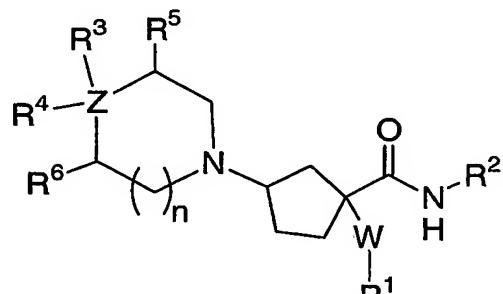
- (g) -CN,
- (h) -NR⁹R¹⁰, and
- (i) -CONR⁹R¹⁰;

5 R⁵ and R⁶ are independently selected from:

- (a) hydrogen,
- (b) hydroxy,
- (c) C₁-6alkyl,
- (d) C₁-6alkyl-hydroxy,
- 10 (e) -O-C₁-3alkyl,
- (f) oxo, and
- (g) halo;

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

15 2. The compound of Claim 1 of the formula Ia:

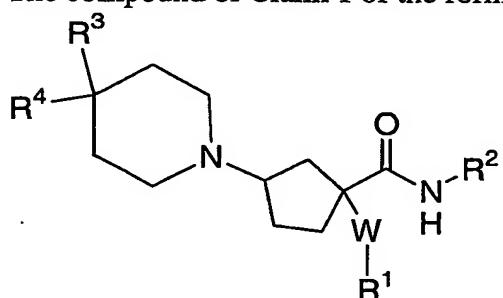


Ia

and pharmaceutically acceptable salts and individual diastereomers thereof.

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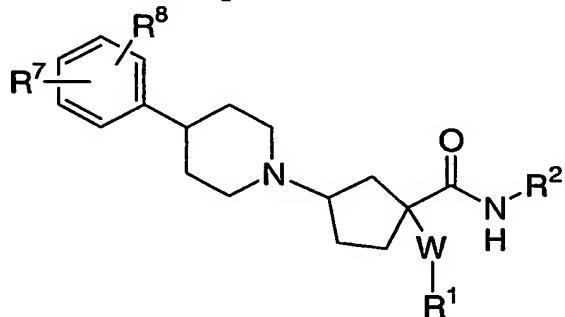
3. The compound of Claim 1 of the formula Ib:



Ib

and pharmaceutically acceptable salts and individual diastereomers thereof.

4. The compound of Claim 1 of the formula Ic:



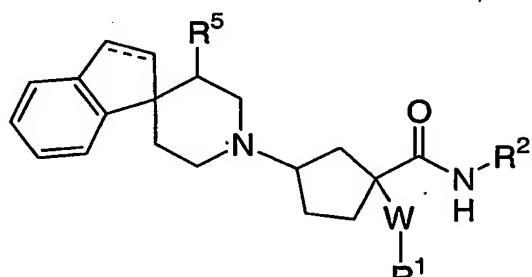
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and wherein R⁷ and R⁸ are independently selected from:

- (a) hydrogen,
- (b) halo,
- (c) trifluoromethyl,
- 10 (d) hydroxy,
- (e) C₁-3alkyl,
- (f) -O-C₁-3alkyl,
- (g) -CO₂H,
- (h) -CO₂C₁-3alkyl, and
- 15 (i) -CN;

and pharmaceutically acceptable salts and individual diastereomers thereof.

5. The compound of Claim 1 of the formula Id:

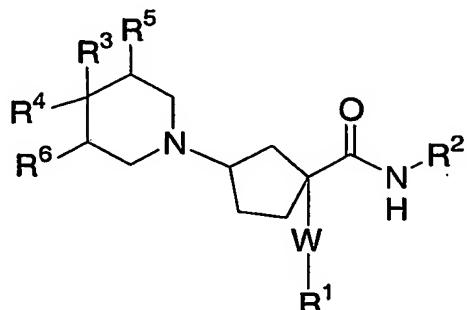


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wherein the dash line represents either single or double bonds;

and pharmaceutically acceptable salts and individual diastereomers thereof.

6. The compound of Claim 1 of the formula:



5

wherein W is selected from furanyl, imidazolyl, oxadiazolyl, oxazolyl, phenyl, pyrazolyl, pyrazinyl, pyridyl, pyridazinyl, pyrimidyl, pyrrolyl, thiadiazolyl, and thiazolyl, and pharmaceutically acceptable salts and individual diastereomers thereof.

10 7. The compound of Claim 1 wherein W is selected from furanyl, imidazolyl, oxadiazolyl, oxazolyl, phenyl, pyrazolyl, pyrazinyl, pyridyl, pyridazinyl, pyrimidyl, pyrrolyl, thiadiazolyl, thiazolyl, thienyl, and triazolyl, and N-oxides thereof.

15 8. The compound of Claim 1 wherein X is -CONH-.

9. The compound of Claim 1 wherein Z is -C-, -N- or -O-.

20 10. The compound of Claim 1 wherein n is 0 and 1.

11. The compound of Claim 1 wherein R¹ is selected from:

- (a) hydrogen
- (b) halo
- (c) C₁₋₃alkyl,
- (d) -O-C₁₋₃alkyl,
- (e) -CO₂R⁹,
- (f) -S-C₁₋₃alkyl,
- (g) -SO₂-C₁₋₃alkyl,

5 (h) $-\text{SCF}_3$,
(i) $\text{NHC}(=\text{NH})\text{NR}^9\text{R}^{10}$
(j) $-\text{NR}^9\text{R}^{10}$,
(k) $-\text{NR}^9\text{-SO}_2\text{-R}^{10}$,
(l) $-\text{SO}_2\text{-NR}^9\text{R}^{10}$, and
(m) $-\text{CONR}^9\text{R}^{10}$.

12. The compound of Claim 1 wherein R^2 is selected from
-(C_{0-4} alkyl)-phenyl and -(C_{0-4} alkyl)-heterocycle,

10 where heterocycle is selected from:

furanyl, imidazolyl, oxadiazolyl, oxazolyl, pyrazolyl, pyrazinyl,
pyridyl, pyridazinyl, pyrimidyl, pyrrolyl, thiadiazolyl, thiazolyl, thienyl,
and triazolyl, and N-oxides thereof,

15 where the alkyl is unsubstituted or substituted with 1-7 substituents where the
substituents are independently selected from:

(a) halo,
(b) hydroxy,
(c) $-\text{O-C}_1\text{-3alkyl}$, and
(d) trifluoromethyl,

20 and where the phenyl or heterocycle is unsubstituted or substituted with 1-5
substituents where the substituents are independently selected from:

(a) halo,
(b) trifluoromethyl,
(c) trifluoromethoxy,
25 (d) hydroxy,
(e) $\text{C}_1\text{-3alkyl}$,
(f) $-\text{O-C}_1\text{-3alkyl}$,
(g) $-\text{CO}_2\text{R}^9$,
(h) $-\text{S-C}_1\text{-3alkyl}$,
30 (i) $-\text{SO}_2\text{-C}_1\text{-3alkyl}$,
(j) $-\text{SCF}_3$,
(k) $-\text{CO}_2\text{R}^9$,
(l) $-\text{NR}^9\text{R}^{10}$,
(m) $-\text{NR}^9\text{-SO}_2\text{-R}^{10}$,

- (n) $-\text{SO}_2\text{-NR}^9\text{R}^{10}$, and
- (o) $-\text{CONR}^9\text{R}^{10}$.

13. The compound of Claim 1 wherein R^2 is selected from
5 $-(\text{C}_0\text{-4alkyl})\text{-phenyl}$ and $-(\text{C}_0\text{-4alkyl})\text{-heterocycle}$,
where heterocycle is selected from: pyridyl, pyridazinyl, and N-oxides thereof,
where the alkyl is unsubstituted or substituted with 1-7 substituents where the
substituents are independently selected from:
10 (a) halo,
(b) hydroxy,
(c) $-\text{O-C}_1\text{-3alkyl}$, and
(d) trifluoromethyl,
and where the phenyl or heterocycle is unsubstituted or substituted with 1-3
substituents where the substituents are independently selected from:
15 (a) halo,
(b) trifluoromethyl,
(c) trifluoromethoxy,
(d) hydroxy,
(e) $\text{C}_1\text{-3alkyl}$,
20 (f) $-\text{O-C}_1\text{-3alkyl}$,
(g) $-\text{CO}_2\text{-C}_1\text{-3alkyl}$,
(h) $-\text{CO}_2\text{H}$,
(i) $-\text{S-C}_1\text{-3alkyl}$,
(j) $-\text{SO}_2\text{-C}_1\text{-3alkyl}$,
25 (k) $-\text{SCF}_3$,
(l) $-\text{NH}_2$,
(m) $-\text{NH-SO}_2\text{-C}_1\text{-3alkyl}$, and
(n) $-\text{SO}_2\text{-NH}_2$.

30 14. The compound of Claim 1 wherein R^2 is selected from
 $-\text{CH}_2\text{-phenyl}$ and $-\text{CH}_2\text{-heterocycle}$,
where heterocycle is selected from: pyridyl, pyridazinyl, and N-oxides thereof,
and where the phenyl or heterocycle is unsubstituted or substituted with 1-3
substituents where the substituents are independently selected from:

- (a) halo,
- (b) trifluoromethyl,
- (c) trifluoromethoxy,
- (d) hydroxy,
- 5 (e) C₁₋₃alkyl,
- (f) -O-C₁₋₃alkyl,
- (g) -CO₂-C₁₋₃alkyl,
- (h) -CO₂H,
- (i) -S-C₁₋₃alkyl,
- 10 (j) -SO₂-C₁₋₃alkyl,
- (k) -SCF₃,
- (l) -NH₂,
- (m) -NH-SO₂-C₁₋₃alkyl, and
- (n) -SO₂-NH₂.

15

15. The compound of Claim 1 wherein R² is selected from:

- (1) -CH₂-(phenyl),
- (2) -CH₂-(4-bromophenyl),
- (3) -CH₂-(3-chlorophenyl),
- 20 (4) -CH₂-(3,5-difluorophenyl),
- (5) -CH₂-((2-trifluoromethyl)phenyl),
- (6) -CH₂-((3-trifluoromethyl)phenyl),
- (7) -CH₂-((4-trifluoromethyl)phenyl),
- (8) -CH₂-((3-trifluoromethoxy)phenyl),
- 25 (9) -CH₂-((3-trifluoromethylthio)phenyl),
- (10) -CH₂-((3-trifluoromethoxy-5-thiomethyl)phenyl),
- (11) -CH₂-((3-trifluoromethoxy-5-methoxy)phenyl),
- (12) -CH₂-((3-trifluoromethoxy-5-methanesulfonyl)phenyl),
- (13) -CH₂-((3-trifluoromethoxy-5-amino)phenyl),
- 30 (14) -CH₂-((3-trifluoromethoxy-5-aminomethanesulfonyl)phenyl),
- (15) -CH₂-((3-trifluoromethoxy-5-sulfonylamino)phenyl),
- (16) -CH₂-((3,5-bis-trifluoromethyl)phenyl),
- (17) -CH₂-((3-fluoro-5-trifluoromethyl)phenyl),
- (18) -CH(CH₃)-((3,5-bis-trifluoromethyl)phenyl),
- 35 (19) -C(CH₃)₂-((3,5-bis-trifluoromethyl)phenyl),

(20) -CH₂-(4-(2-trifluoromethyl)pyridyl),
(21) -CH₂-(5-(3-trifluoromethyl)pyridyl),
(22) -CH₂-(5-(3-trifluoromethyl)pyridazinyl),
(23) -CH₂-(4-(2-trifluoromethyl)pyridyl-N-oxide), and
5 (24) -CH₂-(5-(3-trifluoromethyl)pyridyl-N-oxide).

16. The compound of Claim 1 wherein R³ is hydrogen or phenyl, where the phenyl is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

10 (a) halo,
(b) trifluoromethyl,
(c) hydroxy,
(d) C₁-3alkyl,
(e) -O-C₁-3alkyl,
15 (f) -CO₂R⁹,
(g) -CN,
(h) -NR⁹R¹⁰, and
(i) -CONR⁹R¹⁰.

20 17. The compound of Claim 1 wherein R³ is hydrogen or phenyl, where the phenyl is unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from:

25 (a) halo,
(c) hydroxy,
(d) C₁-3alkyl,
(e) -O-C₁-3alkyl, and
(f) -CO₂R⁹.

30 18. The compound of Claim 1 wherein R³ is phenyl, or para-fluorophenyl.

19. The compound of Claim 1 wherein R⁴ is selected from:
(a) hydrogen,
(b) hydroxy,

- (c) -CO₂H,
- (d) -CO₂C₁₋₆alkyl,
- (e) -CN.

5 20. The compound of Claim 1 wherein R⁵ and R⁶ are independently selected from:

- (a) hydrogen,
- (b) hydroxy,
- (c) -CH₃,
- 10 (d) -O-CH₃, and
- (e) oxo.

15 21. A compound which is selected from the group consisting of the title compounds of the Examples, and pharmaceutically acceptable salts and individual diastereomers thereof.

22. A pharmaceutical composition which comprises an inert carrier and a compound of Claim 1.

20 23. A method for modulation of chemokine receptor activity in a mammal in need thereof which comprises the administration of an effective amount of the compound of Claim 1.

25 24. A method for treating, ameliorating or controlling an inflammatory or immunoregulatory disorder or disease which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1.

30 25. A method for reducing the risk of an inflammatory or immunoregulatory disorder or disease which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1.

26. A method for treating, ameliorating or controlling rheumatoid arthritis which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1.